FORM-PTO-1390 (Rev. 10-96) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 017753-128

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5): Unas 09/601019

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR00/00065	14 January 2000	14 January 1999

TITLE OF INVENTION: COMPOSITION FOR TREATING OBESITY AND ESTHETIC TREATMENT PROCESS

APPLICANT(S) FOR DO/EO/US: Max ROMBI

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and the PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An unexecuted oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:

    Copy of PCT Request (Form PCT/RO/101)

533 Rec'd PCT/PTO 25 JUL 2000

U.S. APPLICATION NO.	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
Unassigned 09/601019	PCT/FR00/00065	017753-128

17. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Search Report has been prepared by the EPO or JPO $840.00 (970)		
International preliminary examination fee paid to USPTO (37 CFR 1.482) $670.00 (956)		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) $690.00 (958)		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO $970.00 (960)		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) $96.00 (962)		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of **$130.00 (154)** for furnishing the oath or declaration later than 20 ☐ 30 ☐ months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	20 -20 =	-0-	X$18.00 (966)	$ -0-	
Independent Claims	3 -3 =	-0-	X$78.00 (964)	$ -0-	
Multiple dependent claim(s) (if applicable)			+$260.00 (968)	$ -0-	
TOTAL OF ABOVE CALCULATIONS =				$ 840.00	
Reduction for 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$	-
SUBTOTAL =				$ 840.00	
Processing fee of **$130.00 (156)** for furnishing the English translation later than 20 ☐ 30 ☐ months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$ 840.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00 (581)** per property +				$	
TOTAL FEES ENCLOSED =				$ 840.00	
				Amount to be: refunded	$
				charged	$

a. ☒ A check in the amount of $ 840.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 02-4800 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-4800. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Norman H. Stepno
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, Virginia 22313-1404

Reg. No. 40,373

SIGNATURE

for Norman H. Stepno
NAME

22,716
REGISTRATION NUMBER

Date: July 25, 2000

(09/99)

Patent
Attorney's Docket No. 017753-128

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Max ROMBI	)	
	)	
Application No.: Unassigned	)	Group Art Unit: Unassigned
	)	
Filed: July 25, 2000	)	Examiner: Unassigned
	)	
For: COMPOSITION FOR TREATING OBESITY AND ESTHETIC TREATMENT PROCESS	)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination on the merits, please amend the above-identified application as follows:

IN THE CLAIMS:

Please amend claims 1-15 as follows:

1. (Amended) [Composition] A composition for the curative and prophylactic treatment of obesity, comprising an extract of green tea containing from 20% to 50% by mass of catechols expressed as epigallocatechol gallate (EGCG).

2. (Amended) [Composition] A composition according to Claim 1, [characterized in that] wherein the extract of green tea contains from 20% to 30% by mass of catechols expressed as epigallocatechol gallate (EGCG).

3. (Amended) [Composition] A composition according to [either of Claims] Claim 1 [and 2, characterized in that], wherein the extract of green tea contains from 5% to 10% by mass of caffeine.

4. (Amended) [Composition] A composition according to [one of Claims] Claim 1 [to 3, characterized in that], wherein the extract of green tea has a ratio of the concentration of catechols to the concentration of caffeine of between 2 and 10.

5. (Amended) [Composition] A composition according to [one of Claims] Claim 1 [to 4, characterized in that], wherein the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg[, preferably about 375 mg,] of catechols per day, and from 50 mg to 200 mg[, preferably about 150 mg,] of caffeine per day.

6. (Amended) [Use of an extract or powder of green tea for the manufacture of] A method of manufacturing a medicinal product which has antilipase and/or thermogenic

properties, and which is intended for the curative and prophylactic treatment of obesity, comprising using an extract or powder of green tea.

7. (Amended) [Use] A method according to Claim 6, [characterized in that] wherein the extract of green tea contains from 20% to 50%[, preferably from 20% to 30%,] by mass of catechols expressed as epigallocatechol gallate (EGCG).

8. (Amended) [Use] A method according to [either of Claims] Claim 6 [and 7, characterized in that], wherein the extract of green tea contains from 5% to 10% by mass of caffeine.

9. (Amended) [Use] A method according to [one of Claims] Claim 6 [to 8, characterized in that], wherein the extract of green tea has a ratio of the concentration of catechols to the concentration of caffeine of between 2 and 10.

10. (Amended) [Use] A method according to [one of Claims] Claim 6 [to 9, characterized in that], wherein the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg[, preferably about 375 mg,] of catechols per day, and from 50 mg to 200 mg[, preferably about 150 mg,] of caffeine per day.

11. (Amended) [Process] A method for the esthetic treatment of a human being in order to enhance his or her figure, [characterized in that it involves] wherein said method comprises the oral administration of a catechol-enriched extract of green tea in order to bring about a loss of weigh or to maintain a weight level which is as low as desired.

12. (Amended) [Process] A method according to Claim 11, [characterized in that] wherein the extract of green tea contains from 20% to 50%[, preferably from 20% to 30%,] by mass of catechols expressed as epigallocatechol gallate (EGCG).

13. (Amended) [Process] A method according to [either of Claims] Claim 11 [and 12, characterized in that], wherein the extract of green tea contains from 5% to 10% by mass of caffeine.

14. (Amended) [Process] A method according to [one of Claims] Claim 11 [to 13, characterized in that], wherein the extract of green tea has a ration of the concentration of catechols to the concentration of caffeine of between 2 and 10.

15. (Amended) [Process] A method according to [one of Claims] Claim 11 [to 14, characterized in that], wherein the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg[, preferably about 375 mg,] of

catechols per day, and from 50 mg to 200 mg[, preferably about 150 mg,] of caffeine per day.

Please add claims 16-20 as follows:

--16. A composition according to Claim 5, wherein the extract of green tea is titrated so as to allow the administration of a daily dose of about 375 mg of catechols per day, and about 150 mg of caffeine per day.

17. A method according to Claim 7, wherein the extract of green tea contains from 20% to 30% by mass of catechols expressed as epigallocatechol gallate (EGCG).

18. A method according to Claim 10, wherein the extract of green tea is titrated so as to allow the administration of a daily dose of about 375 mg of catechols per day, and about 150 mg of caffeine per day.

19. A method according to Claim 12, wherein the extract of green tea contains from 20% to 30% by mass of catechols expressed as epigallocatechol gallate (EGCG).

20. A method according to Claim 15, wherein the extract of green tea is titrated so as to allow the administration of a daily dose of from about 375 mg of catechols per day, and about 150 mg of caffeine per day.--

REMARKS

Entry of the foregoing and favorable consideration of the subject application, in light of the following remarks, are respectfully requested.

By the foregoing amendment, the claims have been amended to remove the multiple dependencies and to place such claims in standard U.S. form. New claims 16-20 contain the subject matter canceled from claims 5, 7, 10, 12 and 15. No new matter has been added by the foregoing amendment.

In the event that there are any questions relating to this Preliminary Amendment, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Susan M. Dadio
Registration No. 40,373

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: July 25, 2000

COMPOSITION FOR TREATING OBESITY AND ESTHETIC TREATMENT PROCESS

The present invention relates to the general field of treating obesity. The invention is directed in particular toward compositions for the curative and prophylactic treatment of obesity, but it also relates to the esthetic treatment of a human being to enhance his or her figure.

The therapeutic objective as regards obesity is well defined: it is a matter either of allowing the individual to lose a significant amount of weight, or of helping the individual to maintain a weight level which is as low as desired.

Several types of approach have been envisaged to date.

Nutritional approaches are directed toward reducing the supply of energy in the form of foods. This can be achieved either by drastically reducing the energy supplies or by replacing high-energy nutrients with others which are lower in energy: such as indigestible substitute fats, structured triglycerides which are difficult to assimilate or dietary fibers which cannot be assimilated.

The therapeutic approaches may have a variety of targets.

· Reducing the food intake may be the first objective. Attempts to reduce the food intake may be made by using anorexigenic substances, whose short-term effects are proven, but whose duration of use is limited on account of adverse side effects. In fact, very few of these products can truly be used and their long-term efficacy remains highly debated. New molecules are undergoing assessment or may do so in the near future, but their value still remains to be shown.

· A second objective may be to increase the expenditure of energy by using thermogenic substances which act at the central or peripheral level. The use of these substances still remains limited.

A third objective is to reduce the assimilation of the dietary lipids, or optionally even that of the carbohydrates. This is a more recent approach, but is gaining in interest. A reduction in the assimilation of the dietary lipids may be obtained either by reducing the activity of the digestive enzymes concerned, or by modifying the properties of the interfaces transporting the lipid molecules, emulsions, vesicles or micelles.

The traditional use of tea is in the form of an infusion, for which the tip of the stems, comprising the last two leaves and the bud, are used. After harvesting, these leaves may be subjected to a fermentation, resulting in a transformation of the chemical substances they contain and in particular the catechols, which corresponds to black tea, or else may be dried immediately, thus giving green tea.

Besides catechols, tea contains caffeine, the diuretic effect of which is well known. This diuretic effect is the reason for the traditional use of green tea as a medicinal plant to promote the elimination of water by the kidneys, either in the case of urinary disorders or as a supplement to weight-reducing diets. The presence of caffeine is also the reason for the traditional use of tea in conditions of fatigue (asthenia).

Numerous epidemiological studies carried out on certain populations have clearly demonstrated the beneficial effects of the chronic ingestion of tea, and more particularly of green tea. Thus, the long-term consumption of green tea is thought to be anti-atherogenic on account of its hypocholesterolemiant effects (Muramatsu et al. 1986, Yang et al. 1997) and its ability to prevent the oxidation of LDLs in the circulation (Tijburg et al. 1997). Green tea is also known for its anti-mutagenic and anti-carcinogenic effects. Thus, it has been shown that green tea significantly reduces the risk of colorectal, skin and breast cancers (Blot et al. 1997, Conney et al. 1997,

Dreosti et al. 1997, Jankun et al. 1997, Ji et al. 1997).

The traditional use of green tea as a diuretic is currently performed in the form of infusions, liquid extracts, extracts of plant powders or extracts in gel capsules or tablets. In these various forms, the green tea, often combined with another diuretic plant, is generally used at a dose corresponding to 1 to 3 g of plant per day.

In the context of screening pharmacological properties of various plants, it has been discovered that extracts of green tea have noteworthy properties which allow them to be used in the treatment of obesity.

The human body continually expends energy in order to function. The origins of this expenditure of energy are threefold: the metabolism, muscular work and thermogenesis, which corresponds to the energy expended by the body to maintain a constant temperature.

The expenditure of energy is compensated for by the energy supplied by the assimilation of foods. If the energy supplied from the dietary ration is strictly identical to the energy expended, the individual maintains a stable weight. If there is an excess supply of energy, the body stores this energy in the form of fats (increase in weight), and if there is a deficit in the supply of energy, the body draws the energy it lacks by burning off the fats stored (loss of weight). However, in this latter situation of an energy deficit encountered in the course of weight-reducing diets, the body reacts to save energy and reduce thermogenesis. This is the control mechanism which accounts for the failure of weigh-reducing diets. Specifically, after losing weight for a few weeks, the individual's weight stabilizes. If they wish to continue to slim, they must further reduce their food intake.

The full value of being able continually to increase thermogenesis, in particular in the course of a low-calorie diet during which it is lowered, may thus

be appreciated. Various chemical substances stimulate thermogenesis, such as nicotine, ephedrine, aspirin, caffeine, etc., but none of them has made it possible to produce a medicinal product for treating obesity since the doses required to obtain an increase in thermogenesis entail considerable side effects, which are incompatible with a treatment which is necessarily long-lasting, generally extending over several months.

This objective has been achieved in accordance with the present invention by means of a composition for the curative and prophylactic treatment of obesity, comprising an extract of green tea, Camellia sinensis, which is rich in catechols.

The present invention is also directed toward the use of an extract or powder of green tea which has anti-lipase and/or thermogenic properties, for the manufacture of a medicinal product intended for the curative and prophylactic treatment of obesity.

Finally, the present invention relates to a process for the esthetic treatment of a human being in order to enhance his or her figure, characterized in that it involves the oral administration of a catechol-enriched extract of green tea in order to bring about a loss of weight or to maintain a weight level which is as low as desired.

In the context of the present invention, the extract of green tea contains from 20% to 50%, in particular from 20% to 30%, by mass of catechols expressed as epigallocatechol gallate (EGCG).

The content of catechols, expressed as epigallocatechol gallate (EGCG), is, for example, advantageously determined in the context of the present invention by using the analytical method described below.

The process is performed by liquid chromatography.

Solution to be examined: 80 ml of methanol R are added to 0.200 g of extract. The mixture is placed under magnetic stirring for 5 min and then in an

ultrasound bath for 5 min. The resulting mixture is filtered through paper and the volume is made up to 100 ml with the same solvent. This solution is diluted fivefold with methanol R.

Caffeine stock solution: 30 mg of caffeine are dissolved in methanol and made up to 100 ml with the same solvent.

Epigallocatechol gallate stock solution: 6 mg of epigallocatechol gallate (EGCG) are dissolved in methanol and made up to 10 ml with the same solvent.

Control solution: 1 ml of each stock solution is taken and made up to 10 ml with the same solvent.

The chromatography can be carried out using:

- a stainless steel column of length 250 mm and inside diameter 4.6 mm, filled with octadecylsilyl silica gel for chromatography R (5 µm) and thermostatically maintained at 20°C (Nucleosil C18) and a precolumn having the same characteristics as the column,
- as mobile phase, at a flow rate of 1 ml/min, a mixture of aqueous 2% V/V glacial acetic acid solution (A) and of acetonitrile (B), the linear elution gradient of which is as follows:

Time (min)	A (%)	B (%)
0	95	5
5	95	5
10	90	10
17	85	15
30	82	18
35	82	18
40	95	5

- as detector, a spectrophotometer set at 278 nm.

10 µl of each of the solutions are injected separately, at least twice. The sensitivity of the detector is adjusted so as to obtain peaks whose height

represents at least 50% of the total scale of the recorder.

The percentage caffeine content is calculated using the following expression:

$$\frac{SCE}{SCT} \times \frac{MCT}{MCE} \times 0.05$$

SCE: area of the peak corresponding to caffeine in the chromatogram obtained with the solution to be examined
SCT: area of the peak corresponding to caffeine in the chromatogram obtained with the control solution
MCE: test sample of extract in the solution to be examined, expressed in grams
MCT: test sample of caffeine in the control solution, expressed in milligrams.

The percentage content of catechols expressed as epigallocatechol gallate (EGCG) is calculated using the following expression:

$$\frac{\Sigma SE}{ST} \times \frac{MT}{ME} \times 0.5$$

ΣSE: sum of the areas of the peaks (2-5-6-7-8) corresponding to catechols in the chromatogram obtained with the solution to be examined
ST: area of the peak corresponding to the EGCG in the chromatogram obtained with the control solution
ME: test sample of extract in the solution to be examined, expressed in grams
MT: test sample of EGCG in the control solution, expressed in milligrams.

It should be pointed out that the epigallocatechol gallate represents on average about 70% of all the catechols present in an extract of green tea, with a range of between 50% and 90%.

According to one particular characteristic of the present invention, the extract of green tea contains from 5% to 10% by mass of caffeine.

According to another characteristic of the invention, the extract of green tea has a ratio of the concentration of catechols to the concentration of caffeine of between 2 and 10.

According to one preferred characteristic of the invention, the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg, preferably about 375 mg, of catechols per day, and from 50 mg to 200 mg, preferably about 150 mg, of caffeine per day.

The increase in thermogenesis in rats by an extract of green tea according to the invention was studied according to the following protocol:

The oxygen consumption of rats, maintained in a hermetic chamber for two hours and more, is measured after administering the test product. Since the expenditure of energy is proportional to the oxygen consumption, this technique makes it possible to measure the increase in thermogenesis, the basal metabolism and the muscular work being constant before and after treatment.

The test product was an extract of green tea containing 24.7% catechols and 8.35% caffeine.

The following results were obtained:

Controls: 0.06 $w/kg^{0.75}$

0.5 mg of extract/kg: 0.45 $w/kg^{0.75}$

1.0 mg of extract/kg: 0.81 $w/kg^{0.75}$

2.0 mg of extract/kg: 1.10 $w/kg^{0.75}$

The increase in thermogenesis in man by an extract of green tea according to the invention was also determined.

A similar study was carried out on 10 volunteers receiving at each meal either 500 mg of an extract of green tea (corresponding to 125 mg of catechols and 50 mg of caffeine), or 50 mg of caffeine, or a placebo.

The total expenditure of energy over 24 h showed a statistically significant increase ($p < 0.01$)

in favor of the extract: 9867 kJ compared with 9538 kJ for the placebo and 9599 kJ for caffeine.

These results demonstrate the ability of an extract of green tea according to the invention to significantly increase thermogenesis. This property is not associated with the caffeine content of the extract, since the administration of caffeine alone, at the same dose as that provided by the extract of green tea, does not increase thermogenesis.

Furthermore, the fact that the significant decrease in the Respiratory Quotient is not accompanied by an increase in the urinary excretion of nitrogen, makes it possible to conclude that there has been an increase in the oxidation of lipids, which is the desired aim in any treatment of obesity.

Finally, it has been possible to demonstrate that the extract of green tea according to the invention leads to an inhibition of the digestive lipases. An in vitro study made it possible to demonstrate that the extract of green tea, at a dose of 6 mg of extract per 100 mg of lipids, partially eliminates the emulsification of the lipids, both in the stomach and in the intestine. As it is known that the emulsification of lipids is the essential step in the action of lipases on food lipids, these results may account for the inhibitory ability of digestive lipases.

Another in vitro study, carried out under conditions reproducing the physiological conditions (successive action on triolein of gastric lipase and then of pancreatic lipase) demonstrated that the extract of green tea, at a dose of 6 mg/100 mg of lipids, allows virtually total inhibition of the gastric lipase (89% inhibition) and partial inhibition of the pancreatic lipase (32% inhibition), i.e. a total inhibition of lipolysis of close to 40%.

The use of a powder of green tea which has an intrinsically lower dose of catechols and/or caffeine, but in a larger amount making it possible to

manufacture a medicinal product which has anti-lipase and/or thermogenic properties, obviously also falls within the context of the present invention.

In the context of the present invention, in vitro studies were carried out to demonstrate the existence of synergy between epigallocatechol gallate and caffeine. These studies were carried out on an ex vivo pharmacological model of thermogenesis. The principle is to measure the oxygen consumption of a sample of rat brown adipose tissue; the oxygen consumption is proportional to the thermogenesis induced in the adipose tissue by the various test substances.

The results below indicate the increase in oxygen consumption as a function of the concentration of EGCG and/or of caffeine.

Caffeine	100 µM	0	0	100 µM	100 µM
EGCG	0	100 µM	200 µM	100 µM	200 µM
Increase in oxygen consumption	no effect	no effect	+ 40%	no effect	+ 140%

These results clearly demonstrate the existence of synergistic stimulation of thermogenesis for a concentration of 200 µM of EGCG and 100 µM of caffeine, i.e. an EGCG/caffeine ratio of 2.

Given the other pharmacological effects of caffeine (tachycardia, insomnia), it may thus be desirable, in order to increase thermogenesis, to limit the amount of caffeine and to increase the EGCG/caffeine ratio. For this reason, according to one advantageous variant of the invention, this ratio will preferably be between 2 and 10.

Example of obtaining an extract of green tea

Green tea contains on average 6% to 7% catechols and 2% to 3% caffeine.

In order to obtain the properties of increasing thermogenesis and of inhibiting digestive lipases which

are described above, a sufficient supply of catechols is necessary. It is thus necessary to carry out an extraction of the green tea making it possible to obtain an extract which is sufficiently concentrated in catechols.

By way of example, the following extraction process can be used: 1 kg of the tips of ground stems, comprising the last two leaves and the bud, of green tea are extracted by percolation for 6 to 8 h with 10 kg of 80% ethanol (m/m). After filtration, the extract is concentrated under partial vacuum at a maximum temperature of 60°C. The concentrated extract is then spray-dried at a maximum temperature of 250°C with or without maltodextrin, depending on the plotter specifications selected. This process gives an extract containing 20% to 30% catechols and 5% to 10% caffeine.

This example is not limiting, and other extraction processes for obtaining an extract which is sufficiently rich in catechols can be used, in particular by varying the proportions of water and ethanol, or by using other solvents such as water, ethyl acetate, methanol, etc., alone or in combination. The choice of solvents selected will make it possible to vary the catechol and caffeine contents, the objective being a high catechol content, since the catechols are the main source of the pharmacological properties demonstrated above.

In this context, the use of green tea which has been partially decaffeinated beforehand by any extraction process which does not have a negative effect on the catechols (for example methylene chloride or supercritical carbon dioxide) may be entirely envisaged in order to obtain a tea extract containing only a small percentage of caffeine.

Without at all wishing to be limited to such an interpretation, it appears likely that the mechanism of activity of the extracts of green tea, which is the subject of the present invention, can be explained as follows. The catechols present in high concentration in

the extracts of green tea according to the invention exert an inhibitory effect on catechol-O-methyltransferase (COMT), whereas the caffeine concentration of the extracts of green tea according to the invention acts by inhibiting phosphodiesterases, which leads to a reinforced activity of noradrenalin on thermogenesis.

CLAIMS

1. Composition for the curative and prophylactic treatment of obesity, comprising an extract of green tea containing from 20% to 50% by mass of catechols expressed as epigallocatechol gallate (EGCG).

2. Composition according to Claim 1, characterized in that the extract of green tea contains from 20% to 30% by mass of catechols expressed as epigallocatechol gallate (EGCG).

3. Composition according to either of Claims 1 and 2, characterized in that the extract of green tea contains from 5% to 10% by mass of caffeine.

4. Composition according to one of Claims 1 to 3, characterized in that the extract of green tea has a ratio of the concentration of catechols to the concentration of caffeine of between 2 and 10.

5. Composition according to one of Claims 1 to 4, characterized in that the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg, preferably about 375 mg, of catechols per day, and from 50 mg to 200 mg, preferably about 150 mg, of caffeine per day.

6. Use of an extract or powder of green tea for the manufacture of a medicinal product which has anti-lipase and/or thermogenic properties, and which is intended for the curative and prophylactic treatment of obesity.

7. Use according to Claim 6, characterized in that the extract of green tea contains from 20% to 50%, preferably from 20% to 30%, by mass of catechols expressed as epigallocatechol gallate (EGCG).

8. Use according to either of Claims 6 and 7, characterized in that the extract of green tea contains from 5% to 10% by mass of caffeine.

9. Use according to one of Claims 6 to 8, characterized in that the extract of green tea has a ratio of the concentration of catechols to the concentration of caffeine of between 2 and 10.

10. Use according to one of Claims 6 to 9, characterized in that the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg, preferably about 375 mg, of catechols per day, and from 50 mg to 200 mg, preferably about 150 mg, of caffeine per day.

11. Process for the esthetic treatment of a human being in order to enhance his or her figure, characterized in that it involves the oral administration of a catechol-enriched extract of green tea in order to bring about a loss of weight or to maintain a weight level which is as low as desired.

12. Process according to Claim 11, characterized in that the extract of green tea contains from 20% to 50%, preferably from 20% to 30%, by mass of catechols expressed as epigallocatechol gallate (EGCG).

13. Process according to either of Claims 11 and 12, characterized in that the extract of green tea contains from 5% to 10% by mass of caffeine.

14. Process according to one of Claims 11 to 13, characterized in that the extract of green tea has a ratio of the concentration of catechols to the concentration of caffeine of between 2 and 10.

15. Process according to one of Claims 11 to 14, characterized in that the extract of green tea is titrated so as to allow the administration of a daily dose of from 250 mg to 500 mg, preferably about 375 mg, of catechols per day, and from 50 mg to 200 mg, preferably about 150 mg, of caffeine per day.

ABSTRACT

The invention relates to a composition for the curative and prophylactic treatment of obesity, comprising a catechol-rich extract of green tea, in particular containing from 20% to 50% by mass of catechols expressed as epigallocatechol gallate (EGCG).

COMBINED DECLARATION AND POWER OF ATTORNEY FOR UTILITY PATENT APPLICATION	Attorney's Docket No. 017753-127

As a below-named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below next to my name;
I BELIEVE I AM THE ORIGINAL, FIRST AND SOLE INVENTOR (if only one name is listed below) OR AN ORIGINAL, FIRST AND JOINT INVENTOR (if more than one name is listed below) OF THE SUBJECT MATTER WHICH IS CLAIMED AND FOR WHICH A PATENT IS SOUGHT ON THE INVENTION ENTITLED:

COMPOSITION FOR TREATING OBESITY AND ESTHETIC TREATMENT PROCESS

the specification of which

(check one) ☐ is attached hereto;

☒ was filed on **JANUARY 14, 2000** as

International Application No. **PCT/FR00/00065**

and was amended on _____;
(if applicable)

I HAVE REVIEWED AND UNDERSTAND THE CONTENTS OF THE ABOVE-IDENTIFIED SPECIFICATION, INCLUDING THE CLAIMS, AS AMENDED BY ANY AMENDMENT REFERRED TO ABOVE;

I ACKNOWLEDGE THE DUTY TO DISCLOSE TO THE OFFICE ALL INFORMATION KNOWN TO ME TO BE MATERIAL TO PATENTABILITY AS DEFINED IN TITLE 37, CODE OF FEDERAL REGULATIONS, Sec. 1.56 (as amended effective March 16, 1992);

I do not know and do not believe the said invention was ever known or used in the United States of America before my or our invention thereof, or patented or described in any printed publication in any country before my or our invention thereof or more than one year prior to said application; that said invention was not in public use or on sale in the United States of America more than one year prior to said application; that said invention has not been patented or made the subject of an inventor's certificate issued before the date of said application in any country foreign to the United States of America on any application filed by me or my legal representatives or assigns more than twelve months prior to said application;

I hereby claim foreign priority benefits under Title 35, United States Code Sec. 119 and/or Sec. 365 of any foreign application(s) for patent or inventor's certificate as indicated below and have also identified below any foreign application for patent or inventor's certificate on this invention having a filing date before that of the application(s) on which priority is claimed:

COMBINED DECLARATION AND POWER OF ATTORNEY	Attorney's Docket No. 017753-127

COUNTRY/INTERNATIONAL	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
FRANCE	**99/00328**	**14 JANUARY 1999**	YES X NO_
			YES_ NO_

I hereby appoint the following attorneys and agent(s) to prosecute said application and to transact all business in the Patent and Trademark Office connected therewith and to file, prosecute and to transact all business in connection with international applications directed to said invention:

William L. Mathis	17,337	Ralph L. Freeland, Jr.	16,110	William C. Rowland	30,888
Peter H. Smolka	15,913	Robert G. Mukai	28,531	T. Gene Dillahunty	25,423
Robert S. Swecker	19,885	George A. Hovanec, Jr.	28,223	Anthony W. Shaw	30,104
Platon N. Mandros	22,124	James A. LaBarre	28,632	Patrick C. Keane	32,858
Benton S. Duffett, Jr	22,030	E. Joseph Gess	28,510	Bruce J. Boggs, Jr.	32,344
Joseph R. Magnone	24,239	R. Danny Huntington	27,903	William H. Benz	25,952
Norman H. Stepno	22,716	Eric H. Weisblatt	30,505	Peter K. Skiff	31,917
Ronald L. Grudziecki	24,970	James W. Peterson	26,057	Richard J. McGrath	29,195
Frederick G. Michaud, Jr.	26,003	Teresa Stanek Rea	30,427	Matthew L. Schneider	32,814
Alan E. Kopecki	25,813	Robert E. Krebs	25,885	Michael G. Savage	32,596
Regis E. Slutter	26,999	Robert M. Schulman	31,196	Gerald F. Swiss	30,113
Samuel C. Miller, III	27,360				

and: _____

Address all correspondence to: Norman H. Stepno
Burns, Doane, Swecker & Mathis, LLP
P.O. Box 1404
Alexandria, Virginia 22313-1404

Address all telephone calls to: Norman H. Stepno at (703) 836-6620.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FULL NAME OF SOLE OR FIRST INVENTOR	SIGNATURE	DATE
ROMBI Max		July 24, 2000
RESIDENCE		CITIZENSHIP
BORDIGHERA, ITALY		**French**
POST OFFICE ADDRESS		
Via Degli Inglesi 49, BORDIGHERA 18022, ITALY		

FULL NAME OF SECOND JOINT INVENTOR, IF ANY	SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		

FULL NAME OF THIRD JOINT INVENTOR, IF ANY	SIGNATURE	DATE
RESIDENCE		CITIZENSHIP
POST OFFICE ADDRESS		

(1/96)